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DIABETES

Prevalence, incidence and mortality of type 2 diabetes mellitus revisited: A prospective population-based study in The Netherlands (ZODIAC-1)

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Abstract. *Background*: To present actual data to estimate prevalence, incidence and mortality of known type 2 diabetes mellitus in all age categories in The Netherlands. *Methods*: Prospective population-based study between 1998 and 2000 in The Netherlands. Baseline population of 155,774 patients, registered with 61 general practitioners participating in the Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC)-study. *Results*: Age- and sex-adjusted prevalence of type 2 diabetes was 2.2% at baseline and 2.9% after 2 years of follow-up; for women and men it was 3.1 and 2.7% at follow-up, respectively. Patients aged >70 years account for almost 50% of all type 2 diabetes patients. Age- and sex-adjusted mean annual incidence per 10,000 over 3 years was 22.7 overall; for women 23.1 and for men 22.2. Incidence – even though high – decreases after the age of 70 years. The mortality rate was 47.9/1000 and standardised mortality ratio 1.40. Based on these results, the estimated total number of subjects known with type 2 diabetes was 466,000 for The Netherlands in 2000; the number of patients with newly diagnosed diabetes 36,000. *Conclusions*: Prevalence and incidence rates exceed all estimates regarding known type 2 diabetes for The Netherlands. Elderly patients, aged 70 years and over, account for 50% of the type 2 diabetic population. These results are important for health-care planning.

Key words: Age groups, Diabetes mellitus, Incidence, Mortality, Prevalence, Prospective study, Type 2

Abbreviations: ADA = American Diabetes Association; CI = confidence interval; GP = general practitioner; SD = standard deviation; SMR = standardised mortality ratio; SPSS = Statistical Package for Social Sciences; UK = United Kingdom; US = United States of America; WHO = World Health Organisation; ZODIAC = Zwolle Outpatient Diabetes project Integrating Available Care

Introduction

Type 2 diabetes mellitus is a chronic disease, leading to considerable morbidity and premature mortality [1, 2]. The prevalence is high, especially in the elderly, and increasing [3]. Accurate information about the prevalence of known type 2 diabetes and the number of newly diagnosed cases in the community is essential for health-care planning. In The Netherlands, estimates on current and future incidence, prevalence and mortality are available, based on various studies [4–9]. However, the data used originate from 1993 or earlier, estimates on incidence and prevalence vary considerably [8], and few studies describe older age categories in detail. This variation in estimates on current and future incidence and prevalence may be explained by the differences in models used for future projections, by the year the data used for these projections originate from, and also by differences in the design of studies supplying original data for these estimates. Between studies with a different study design – using oral glucose tolerance tests or based on self report or general practice registers – the large proportion of patients with type 2 diabetes that is presumed to be undiagnosed (and could be as high as 50%) [10, 11] can give rise to varying findings, especially because this proportion again may vary between regions or countries. Not only national but also international literature presents few publications with detailed data on the highest age categories: these publications are difficult to compare because of considerable differences in definitions and study design, and they show highly varying prevalence rates [12–19]. As the prevalence of type 2 diabetes increases quickly and is estimated to be highest in the eldest age categories, we consider it important not to ignore this age category and to present actual data on current prevalence, incidence and mortality of known diabetes in all age groups, including these eldest. These data could be used to describe temporal trends and can support health-care planning. Therefore, in the light of all the above arguments, the aim of this study

is to present actual data from a large population in order to be able to estimate current prevalence, incidence and mortality of type 2 diabetes, as known in or identified through the normal health-care processes, in all age categories in The Netherlands.

Methods

The Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC)-study investigates the effects of a shared-care project for type 2 diabetes. In this project general practitioners (GPs) receive support from diabetes specialist nurses for the practical implementation of the national guidelines with respect to performing the annual control and education in patients with known diabetes. This working protocol does not, in any way, aim to influence in the actual process of diagnosing diabetes and screening high-risk populations; so (changes in) prevalence and incidence are considered comparable with those found in the normal health-care process. In the project, 61 GPs from an eastern part of the country participate. These are all the GPs of the 8 GP-working groups covering the project target area. A GP-working group consists of GPs – with practices in the same town or city – collaborating mainly with respect to delivering medical service in out-of-office hours. GPs could only participate in the project with their total working-group, and all groups invited agreed to participate. This means that among participating GPs there are some with a special interest and others with no special interest in diabetes. In The Netherlands, virtually each inhabitant is registered with a GP.

As part of the ZODIAC-study, we collected cross-sectional data on the general population and all patients with diabetes, as registered with the 61 GPs, in three consecutive years: 1998–2000. Lists naming all patients known with type 2 diabetes, as defined by the national guidelines of the Dutch College of GPs of 1989 and 1999 (based on the 1985 World Health Organisation (WHO) and 1997 American Diabetes Association (ADA) criteria, respectively), were provided annually by the GPs and checked for each individual practice by the principal investigator. These lists were composed combining information on glucose measurements, HbA1c, use of diabetes medication and special markers for signalling diabetes in the patient files. A manual check, consisting of a review of the complete paper and/or electronic patient file, for the validity of the diagnosis, the type of diabetes, and the date of diagnosis was performed by the principal investigator of the study for each individual patient with diabetes in each practice. Patients with type 1 diabetes, defined by age at diagnosis as <40 years and requiring insulin within 1 month of diagnosis, were removed from the lists. The validity of the diagnosis type 2 diabetes was checked in the individual patient files by looking up the glucose measurements the diagnosis was based upon, and comparing these measurements with the criteria for diabetes in the national guideline at the time of diagnosis for each patient. Incident cases (newly diagnosed cases) were defined as having a diabetes duration of <1 year at baseline or in the first or second study year. The total general population, registered with the participating 61 GPs at baseline, consisted of 155,774 persons. The practices had computerised patient lists and all supplied the total number and age- and sex-distribution of the total general population registered with their practice in each study year.

To extrapolate our findings for the Dutch population, we used national data on age- and sex-distribution from the Central Bureau for Statistics for each year corresponding with the study years [20]. To check the external validity of the data, the age- and sex-distribution of the study population and national population were compared. Prevalence rates were calculated as percentages per 5- and 10-year age category. The 95% confidence intervals (CI) for differences between observed proportions were calculated for each age category. Incidence rates were calculated per 10,000 per 5- and 10-year age category. Standardised mortality ratios (SMRs) were calculated for patients with known type 2 diabetes, dividing the observed number of diabetic deaths by the number of expected deaths in the general population, using the Dutch 1998 population as the reference population [20]. Expected numbers were calculated per 5-year age category.

This study was approved by the Medical Ethics Committee of the Isala Clinics (formerly Weezenlanden Hospital).

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, version 8.0.1).

Results

The age and sex distribution of the total general population studied was marginally different from the national population, mainly in the age categories 20–29 and 65–69 years (Figure 1). In these categories the difference between the proportions of the age categories from the total study population and the national population was 2.2 and 0.4%, respectively.

Prevalence

At baseline, 3369 patients known with type 2 diabetes were identified in the total population of 155,774 persons. The mean age of the diabetic population was 67.7 years (standard deviation SD: 12.6) overall, and 69.7 (SD: 12.3) vs. 65.1 (SD: 12.3) for women and men, respectively. Age ranged from 19 to 102 years.

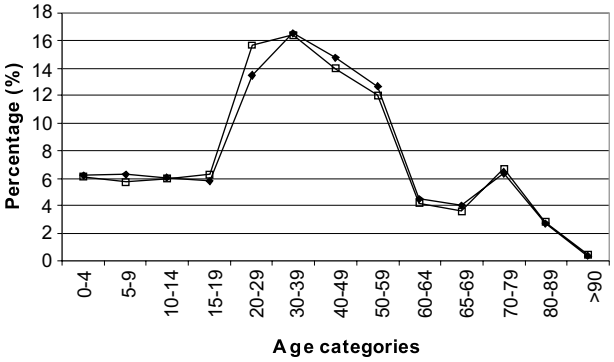

Figure 1. Age and sex distribution of the study population and national population. The Netherlands –♦–, General population study area –□–.

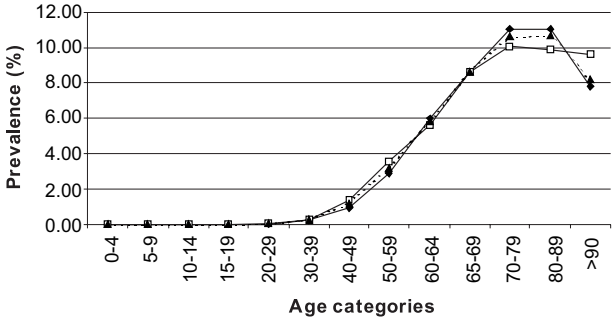

Figure 2. Prevalence of type 2 diabetes at baseline. Total –▲–, Women –♦–, Men –□–.

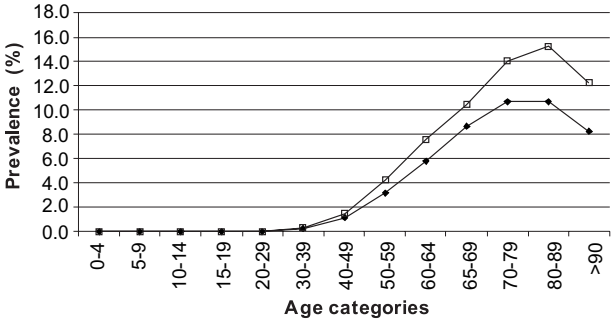

Figure 3. Prevalence per 5- and 10-year age category at baseline and after 2 years. Baseline –♦–, After two follow-up years –□–.

The overall crude prevalence was 2.16%; the age- and sex-adjusted prevalence for The Netherlands was 2.21% (95% CI: 2.13–2.28). Prevalence for women was 2.4 vs. 2.0% in men. The prevalence per age category is presented in Table 1 and Figures 2 and 3. The highest prevalence was found in the age category 70–79 for both women and men. After 2 years of follow-up, the population on the lists of participating GPs consisted of 156,074 persons; the number of participating GPs did not change, but the general population of the practices had grown in the study period, as in the rest of The Netherlands. Because of this change, data on age and sex distribution of the general population of each specific study year were used for the age- and sex-adjustment. In this general population, 4423 patients were known with type 2 diabetes after two follow-up years. Crude prevalence had increased to 2.83% overall, age- and sex-adjusted prevalence to 2.94% overall, to 3.1% for women and to 2.7% for men. For the diabetes population this meant an increase of 33% (women 30%, men 37%) in 2 years. The age distribution for known type 2 diabetes for the male population shifted towards the pattern of the female population. The number of

Table 1. Prevalence per 5- and 10-year age categories for men and women

	Baseline		Follow-up year 2				Increase in prevalence after 2 years	
				Prevalence (%)				
Age categories	Total N	Prevalence (%)	Total (N)	Total	Women	Men	Absolute difference (%)	95% CI
0–4	0	0.0	0	0.0	0.0	0.0	0.00	0.00–0.00
5–9	0	0.0	0	0.0	0.0	0.0	0.00	0.00–0.00
10–14	0	0.0	0	0.0	0.0	0.0	0.00	0.00–0.00
15–19	1	0.0	1	0.0	0.0	0.0	0.00	−0.03–0.03
20–29	8	0.0	8	0.0	0.0	0.0	0.00	−0.04–0.03
30–39	63	0.3	76	0.3	0.3	0.3	0.05	−0.04–0.14
40–49	249	1.2	314	1.5	1.3	1.6	0.29	0.08–0.50
50–59	587	3.2	778	4.3	3.6	4.9	1.05	0.67–1.43
60–64	370	5.8	480	7.5	7.0	8.1	1.73	0.91–2.56
65–69	477	8.6	576	10.4	10.4	10.4	1.77	0.75–2.79
70–79	1091	10.7	1437	14.0	14.1	13.9	3.35	2.43–4.27
80–89	466	10.7	667	15.3	15.4	15.1	4.59	3.17–6.02
>90	57	8.2	86	12.3	12.6	11.1	4.05	0.81–7.30
Total	3369	2.16	4423	2.83	3.08	2.57	0.67	0.56–078

Table 2. Incidence per 10,000 for 5- and 10-year age categories for men and women

Age categories	Newly diagnosed (N)			Mean annual incidence					
	Baseline	1st follow-up year	2nd follow-up year	Total	95% CI	Women	95% CI	Men	95% CI
0–4	0	0	0	0	0–0	0	0–0	0	0–0
5–9	0	0	0	0	0–0	0	0–0	0	0–0
10–14	0	0	0	0	0–0	0	0–0	0	0–0
15–19	0	0	1	0	0–0	1	1–1	0	0–0
20–29	2	1	3	1	1–1	1	1–1	1	1–1
30–39	8	8	5	3	3–3	3	3–3	3	2–3
40–49	19	29	35	13	12–13	13	13–14	12	12–12
50–59	69	88	92	46	45–47	41	40–43	47	46–49
60–64	36	53	48	71	68–74	68	64–72	72	68–76
65–69	42	58	55	91	87–95	87	82–92	97	91–103
70–79	76	103	92	87	84–91	80	76–83	96	91–101
80–89	36	34	31	76	72–80	73	69–78	84	76–91
>90	2	2	2	29	25–33	36	31–41	0	0–0
Total	290	376	364	22.0	21.8–22.2	22.5	22.2–22.7	21.6	21.3–21.8

patients in The Netherlands in 2000, according to the prevalence found, is estimated to be 466,000.

Incidence

The number of patients with newly diagnosed type 2 diabetes at baseline and in year 1 and 2 are shown in Table 2. The overall crude mean annual incidence was 22.0/10,000 and the age- and sex-adjusted incidence 22.7/10,000 (95% CI: 22.5–22.9). For women this was 23.1 and for men 22.2/10,000. The highest incidence for both women and men was found in the age category 65–69, where it was 87 and 97/10,000 per year, respectively. Based on the incidence found, the annual number of patients with newly diagnosed diabetes is estimated to be approximately 36,000 per year in The Netherlands.

Mortality

From the baseline population (n = 3369), 323 (9.6%) patients died during the 2-year follow-up period. The mean age of these patients was 79.3 years (SD: 10.5, range 38–104 years), for women (54.2%) this was 81.5 and for men 76.8 years. The mortality rate was 47.9/1000 for the diabetic population and 8.8/1000 for the total general population in 1998. The SMR for the total diabetic population is 1.40, for women 1.41 and for men 1.44, as compared to the general population. The relative mortality risks per age category are shown in Table 3.

Elderly population

In the population aged 70 years and older, prevalence is higher than in any other age category. Patients aged 70 years and over account for almost half (49.5%) of the total type 2 diabetes population. There is an increase in prevalence with age until the age of 80 at baseline and until the age of 90 after 2 years of follow-up. After the age of 90, prevalence decreases. The largest absolute increase in number of patients with known type 2 diabetes was found in the age category 70–79; the largest absolute increase in prevalence was found in the age category 80–89. The incidence – even though still high between the age of 70–90 years – decreases after a peak at the age of 65–69.

Discussion

Main results

Our study, which is limited to known type 2 diabetes, presents actual data from a large population to estimate current prevalence, incidence and mortality in The Netherlands; our main conclusion is that the prevalence is considerably higher than described or estimated up till now. This is the case for both the overall prevalence [6, 21] and for the prevalence in all different age categories [11, 22–24]. Incident cases explain a part of the rise in prevalence. The incidence we found is also higher than what has been published for The Netherlands up to now, overall as well as for the different age categories [6, 25], except for 30–39 and 80–89 years [4]. From the original population 4.8% died annually. In the elderly population, aged 70 years and over, prevalence is higher than in any other age category; this patient category accounts for almost 50% of all type 2 diabetes patients. Incidence – even though still high between the age of 70–

Table 3. SMRs per 5-year age category

Age categories	Diabetic deaths in two follow-up years N			SMR					
	Women	Men	Total	Women	95% CI	Men	95% CI	Total	95% CI
35–39		1	1	0.00	0.00–0.00	26.46	−46.87–99.78	14.20	−25.17–53.58
40–44	1	1	2	8.36	−14.81–31.54	6.13	−10.86–23.11	7.09	−6.81–20.99
45–49	2	0	2	8.77	−8.42–25.96	0.00	0.00–0.00	2.69	−2.58–7.96
50–54	0	2	2	0.00	0.00–0.00	1.51	−1.45–4.47	1.05	−1.00–3.10
55–59	2	9	11	1.32	−1.26–3.90	3.48	0.26–6.70	2.68	0.44–4.92
60–64	5	7	12	1.73	−0.41–3.87	1.50	−0.07–3.06	1.56	0.31–2.81
65–69	7	10	17	1.15	−0.05–2.35	0.97	0.12–1.82	1.02	0.33–1.70
70–74	24	29	53	1.86	0.81–2.91	1.50	0.73–2.27	1.64	1.01–2.26
75–79	29	26	55	1.28	0.62–1.95	1.12	0.51–1.73	1.16	0.73–1.60
80–84	35	34	69	1.24	0.66–1.82	1.76	0.92–2.59	1.40	0.94–1.87
85–89	40	20	60	1.47	0.83–2.12	1.42	0.54–2.30	1.44	0.93–1.96
90–94	17	6	23	1.33	0.44–2.23	1.02	−0.13–2.17	1.25	0.53–1.96
>95	13	3	16	1.43	0.33–2.54	1.93	−1.16–5.01	1.50	0.46–2.53
Total	175	148	323	1.41	1.11–1.70	1.44	1.11–1.76	1.40	1.18–1.61

89 years – decreases after a peak at the age of 65–69. The current detailed data on prevalence and incidence of known type 2 diabetes in general, and specifically in the elderly, are new for The Netherlands and can support health-care planning in our ageing population. The detailed data on the eldest patients are also important for international comparisons as data on these specific age categories are scarcely available.

Limitations

The main limitation of our study is the lack of knowledge regarding undiagnosed diabetes. The number of undiagnosed patients may be as high as 50% [10, 11]. This group of patients explains the difference in prevalence data between epidemiological studies with different designs: studies using oral glucose tolerance tests to screen populations detect also patients with diabetes who were undiagnosed until that moment, and studies using registers from GPs or surveys do not. The size of this group of undiagnosed patients again might vary between regions or countries, explaining the differences found between studies of the same design in different locations. Due to the extra attention of all care providers regarding the detection of diabetes and the screening of high-risk populations, the percentage of undiagnosed diabetes may have decreased in The Netherlands the past years, as was found in the United States of America (US) as well [26, 27]. To get an idea of the magnitude of the uncertainty regarding the percentage of unknown diabetes, we compared our incidence rates with those from an epidemiological study performed earlier elsewhere in The Netherlands, using oral glucose tolerance tests. They found a cumulative incidence of 6.1–6.9% in the population aged 50–75 at baseline (according to WHO-85 criteria), with a mean follow-up duration of 6.4 years [28]. Our data show a mean annual incidence for this age category which is 31–44% lower. This suggests that there may still be a large group of patients with undiagnosed type 2 diabetes in our population, even though this group may be decreasing.

Another limitation is that the rise in prevalence may partly be explained by the introduction of the revised guidelines of the Dutch College of GPs in 1999 [29]. In these guidelines the 1997 ADA criteria are used for the diagnosis of type 2 diabetes instead of the 1985 WHO criteria in the guidelines used until that moment [30]. Given these criteria, the prevalence of diabetes mellitus among the general Dutch population will change only slightly, but the number of persons to be classified in a different category after their introduction is considerable: 39% of the ADA diabetics are not diabetics according to the current WHO classification, while 38% of the WHO diabetics are not diabetics according to the ADA criteria [31]. The latter group may still be registered as having diabetes in the GP registers, causing a higher prevalence.

Another explanation for the high prevalence of known type 2 diabetes found in our region, as compared to other data derived from GP registers, may be the long-standing attention for diabetes care in the area studied. Moreover, the increase in prevalence may be explained by the extra attention for diabetes care because of the shared-care project. Part of the data used for this study was collected within the scope of this project. On the other hand, over 70 shared-care diabetes initiatives have been described in The Netherlands: the above effect on prevalence of known type 2 diabetes may be found in other places as well [32]. A finding supporting the above

theory is that the increase in prevalence is partly explained by the improvement in GP-registrations during the follow-up years. Patients who were diagnosed, but not yet registered correctly up until that moment, explained almost 40% of the rise in prevalence (in the first follow-up year 40% and in the second 38%). This phenomenon was also found in another Dutch study that showed that it took 10 years of continuous attention for the disease and its registration before the reservoir of unregistered patients was empty [33]. In our opinion, after 3 years of annually composing diabetes lists, combining information on glucose measurements, HbA1c, use of diabetes medication, and special markers for signalling diabetes in the patient files, and after annual extensively checking the lists manually in each practice, the proportion of unregistered known patients with diabetes will be reduced to a minimum. Moreover, the patients with diabetes we found, are all true cases of type 2 diabetes: by checking all individual patient files, we know that no false positive cases were included.

Comparison to other national and international studies

Prevalence

As already stated, our main conclusion is that the prevalence of known type 2 diabetes is higher than described for The Netherlands up till now for both the overall prevalence [6, 21] and for the prevalence in all different age categories [11, 22–24]. The most recent prevalence estimate from Baan et al. [6] was 2.7–3.2% for the population aged >30, whereas we find 4.7% for this age category. However, our prevalence rates of known type 2 diabetes do not yet reach the prevalence of combined diagnosed and undiagnosed diabetes, as found in earlier epidemiological studies, showing that undiagnosed diabetes is still present. Our prevalence is approximately 75% of the prevalence found in Hoorn [11] and in Rotterdam [22]. The estimated number of 466,000 patients with known type 2 diabetes in 2000 exceeds all current and future projections for The Netherlands [6, 7, 9, 23]. Projections from the nineties regarding the increase in the next 15–20 years, vary between 20 and 50%. We found an increase of 33% in 2 years. The overall prevalence of known type 2 diabetes is higher in women than in men, as shown in other studies [11, 22], but lower for women aged <64 which was also shown by Mooy et al. [11] and Han et al. [34]. Prevalence rises sharply in the two follow-up years. The largest absolute increase in known type 2 diabetes is found in the age group 70–79 and not between 45 and 65 as was predicted [7].

As compared to international prevalence rates we find a higher overall prevalence (2.9%) in The Netherlands than in Italy (2.5%) and the United Kingdom (UK) (2.0%) [35, 36], and this also applies for the different age categories in these countries [37, 38]. In the US, the overall prevalence among white non-Hispanics is higher in most publications: for the population aged >20, Harris et al. [27] found a prevalence of 4.8% and Mokdad et al. [39] found 5.9%, vs. 3.9% in this age category in our results.

Incidence

Incident cases explain a part of the rise in prevalence. The incidence we found is higher than what has been published up till now for The Netherlands, overall as well as for the different age categories [6, 25], except for 30–39 and 80–89 years [4].

As compared to international incidence rates we find a higher overall incidence (2.27/1000) than in the UK (1.63/1000) [36]. Compared to our data, the numbers found for the US are too divergent to allow for a valid conclusion [40, 41].

Mortality

From the original population 4.8% died annually. Baan et al. [5] estimated the number of diabetic deaths as a percentage of the total number of deaths to be 18.1% for women and 11.9% for men. According to our results this is lower: 13.1 and 11.4%. This might be explained by the fact that the estimates from Baan et al. [5] are based on mortality ratios from the Verona Study (Italy): these are higher for every age category than the mortality ratios we observed, especially for women [35]. In a Dutch study, De Grauw et al. [42] found a mortality ratio of 1.62 and 1.56 for women and men, respectively, as compared to 1.41 and 1.44 in our results. This might be explained by the difference in study design: we compared to the total general population (including patients with diabetes) whereas they compared to matched cases from the non-diabetic population.

As compared to international data, we find a higher mortality rate (47.9/1000) than in the UK (41.8/1000) [43]. In the US mortality rates for the population aged >65 years are comparable to ours [44]. In an international meta-analysis the percentage of patients dying annualy was found to be lower (3.8%) than in our results (4.8%) [45].

Elderly

No detailed Dutch data on prevalence in the age category >90 years were found but up until the age of 90 the prevalence rates of known diabetes we found are a lot higher than in earlier research, even though the pattern of an initially increasing prevalence that decreases in the eldest patients is similar [11, 22]. Compared with the US, we found a higher prevalence in the eldest age categories (>70 and >75 years for different studies, respectively) [27, 39, 46]. Incidence – even though high between the age of 70–90 years – decreases after a peak at the age of 65–69. For women between 80 and 89 years, we found a lower incidence than others did: 73/10,000 vs. an estimated 103/

10,000 by Barendregt et al. [4]. The Dutch Sentinel Practice Network found a peak between 65 and 79 years [25]. The estimated incidence by others shows a continuous rise without a peak [4, 6].

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